PATENT
ATTORNEY DOCKET NO. 04844/005005

Certificate of Mailing: Date of Deposit: July 24, 2003

I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Moya Kinnealey
Printed name of person mailing correspondence

Moya Kinnealey
Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | |
|---|---|---|---|
| Applicant: | Rima Rozen | Art Unit: | 1634 |
| Serial No.: | 09/931,795 | Examiner: | Carla J. Myers |
| Filed: | August 16, 2001 | Customer No.: | 21559 |
| Title: | METHODS FOR SELECTING A THERAPY FOR A SUBJECT SUFFERING FROM SCHIZOPHRENIA | | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Claims Pending After Entry of Amendment Pursuant to 37 C.F.R. § 1.121(c)(3)

29. A method for selecting a safe and/or efficacious therapy for a subject suffering from a schizophrenia, said method comprising the steps of:

(a) analyzing the MTHFR nucleic acid in a sample obtained from said subject;

(b) determining the presence of a heterozygous C/T mutation at position 677 of MTHFR in said subject, wherein the presence of said mutation is indicative of the safety or efficacy of a therapy; and

(c) selecting a safe or efficacious therapy for said subject.

31. The method of claim 29, wherein said nucleic acid with said mutation at position 677 encodes an MTHFR protein with reduced activity or reduced thermal stability.

32. The method of claim 29, wherein said nucleic acid with said mutation at position 677 further comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

33. The method of claim 32, wherein said nucleic acid with said mutation at position 677 comprises an A/C mutation at position 1298.

34. The method of claim 29, wherein said subject is determined to comprise at least two MTHFR mutations at a position other than 677.

35. The method of claim 34, wherein said mutations at a position other than 677 comprise at least one of a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at

position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

36. The method of claim 35, wherein said mutations at a position other than 677 comprise an A/C mutation at position 1298.

37. A method for determining whether an MTHFR mutation is indicative of the safety or efficacy of a therapy for a schizophrenia, said method comprising the steps of:

(a) determining whether said response of a first subject or set of subjects at increased risk for or diagnosed with said schizophrenia differs from said response of a second subject or set of subjects at increased risk for or diagnosed with said schizophrenia;

(b) analyzing the MTHFR nucleic acid in a sample obtained from said first subject or set of subjects and said second subject or set of subjects; and

(c) determining whether a heterozygous C/T mutation at position 677 of MTHFR differs between said first subject or set of subjects and said second subject or set of subjects, wherein the presence of said mutation is correlated to the safety or efficacy of said therapy, thereby determining whether said mutation is indicative of the safety or efficacy of said therapy.

39. The method of claim 37, wherein said nucleic acid with said mutation at position 677 encodes an MTHFR protein with reduced activity or reduced thermal stability.

40. The method of claim 37, wherein said nucleic acid with said mutation at position 677 further comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

41. The method of claim 40, wherein said nucleic acid with said mutation at position 677comprises an A/C mutation at position 1298.

42. The method of claim 37, wherein said subject is determined to comprise at least two mutations at a position other than 677.

43. The method of claim 42, wherein said mutations at a position other than 677 comprise at least one of a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at

position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

44. The method of claim 43, wherein said mutations at a position other than 677 comprise an A/C mutation at position 1298.

45. A method for preventing, delaying, or treating a schizophrenia in a subject, said method comprising the steps of:

(a) analyzing the MTHFR nucleic acid in a sample obtained from said subject;

(b) determining the presence of a heterozygous C/T mutation at position 677 of MTHFR in said subject, wherein the presence of said mutation is predictive of the safety or efficacy of at least one anti-psychotic therapy;

(c) determining a preferred therapy for said subject, wherein said preferred therapy is efficacious, safe, and/or has reduced toxicity compared to another therapy for schizophrenia; and

(d) administering said preferred therapy to said subject.

47. The method of claim 45, wherein said nucleic acid with said mutation at position 677 encodes an MTHFR protein with reduced activity or reduced thermal stability.

48. The method of claim 45, wherein said nucleic acid with said mutation at position 677 further comprises a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

49. The method of claim 48, wherein said nucleic acid with said mutation at position 677 comprises an A/C mutation at position 1298.

50. The method of claim 45, wherein said subject is determined to comprise at least two mutations at a position other than 677.

51. The method of claim 50, wherein said mutations at a position other than 677 comprise at least one of a G/A mutation at position 167, a G/A mutation at position 482, a C/T mutation a position 559, a C/T mutation at position 692, a C/T mutation at position 764, a G/A mutation at position 792+1, a C/T mutation at position 985, a C/T mutation at position 1015, a C/T mutation at position 1081, an A/C mutation at position 1298, or a T/C mutation at position 1317.

52. The method of claim 51, wherein said mutations at a position other than 677 comprise an A/C mutation at position 1298.

Add the following new claims 53-55.

53. The method of claim 29, further comprising the step of determining the presence of at least one MTHFR mutation at a position other than 677 prior to step (c).

54. The method of claim 37, further comprising determining whether at least one MTHFR mutation at a position other than 677 differs between said first subject or set of subjects and said second subject or set of subjects.

55. The method of claim 45, further comprising determining the presence of at least one MTHFR mutation at a position other than 677 prior to step (c).